Finding a "Missing Link": The Potential of Atoh8 in Hereditary Hemochromatosis, Anemia, and Other Iron-Related Diseases

Nijim, Sally

Disorders of iron metabolism are closely related to human disease. As per the World Health Organization, more than 2 billion worldwide (greater than 30% of the world's population) suffer from anemia due to iron deficiency and more than one million in the United States are afflicted with hereditary hemochromatosis. Further, as profound changes in iron homeostasis accompany inflammation, understanding the mechanisms by which iron metabolism is regulated is critical to stopping infection and inflammation – characteristics commonly and closely associated with many types of human disease. However, the mechanisms by which iron metabolism and erythropoiesis regulate hepcidin – the master iron hormone – are not completely understood, particularly under such stresses as hereditary hemochromatosis and anemia. Recent evidence implicates the transcription factor Atoh8 as a contributor to the regulation of hepcidin. As signaling to hepcidin via transferrin involves the molecules HFE and TFR2, we measured parameters of iron status in wild type mice and mice in which the HFE/TFR2 genes have been disrupted. Ultimately, our results suggested that HFE/TFR2 contribute to the regulation of Atoh8 which participates in hepcidin regulation as a "missing link" in the iron regulatory pathway. Such findings present potential therapeutic targets for treatment of iron-related disorders such as hereditary hemochromatosis and anemia. As there is a relationship between iron status and human susceptibility to infections, this study also advances our understanding of iron metabolism via Atoh8 and is vital in stopping human infection and inflammation, ultimately reducing the need for antibiotics in light of emergence of antibiotic-resistant infections.

Awards Won: